INFLUENCE OF THE MALE IN THE PRODUCTION OF HUMAN TWINS[1]

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IT is frequently pointed out that the father of twins can have little influence in determining their production; such production is purely a maternal quality, due to double ovulation. One possible way, however, in which the male may influence twin production is recognized, but this affects only 1-egg twins. Thus, if we assume that 1-egg twins are due to an early fission of the embryonic blastodisc, or if they are due to a secondary budding (following the method of the armadillo), then the sperm cell might carry the tendency to such fission or budding, as well as the egg cell. This possibility, however, does not help the statistical student of plural births, such as Weinberg, because he believes that the tendency to 1-egg twins is not inherited at all.

In the following study, there will be considered only the class of cases showing heredity most clearly, namely, those in which the principal fraternity under consideration has more than one pair of twins. Parents of such fraternities are spoken of in what follows as repeater fathers or mothers. Our query is then: "What is the relative importance in twinning of inheritance from the maternal and paternal sides, or what is the relative occurrence of twin labors in the close relatives of repeating mothers and of their husbands?"

To get an answer to this question, all available figures on twin repeaters were studied statistically. Of 355 labors occurring to the mothers of repeating mothers, 16 (4.5 per cent.) were twin labors. Of 289 labors occurring to the mothers of twin-repeating fathers, 12 (4.2 per cent.) were twin labors. These statistics thus indicate

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that the frequency of twins in the fraternities of fathers of twins is almost the same as that of twins in the fraternities of mothers of twins. Since the average proportion of labors which are twin labors is 1.1 per cent. for the population as a whole, we see that twins occur in the fraternities of repeating fathers as well as repeating mothers about four times as frequently as in the population as a whole.

To make use of more extended pedigrees, we may compare the tendency to have twin children on the part of *sisters* of the father and the mother of twin fraternities and on the part of *brothers* of the fathers and mothers of such fraternities. Then we obtain the results shown in the following table:

	Per. Cent. of Births that are Twin Births
Father's sisters' children	8.2
Mother's sisters' children	5.5
Father's brothers' children	6.5
Mother's brothers' children	4.5

From this table, most of the items of which were based upon ten or more twin labors, it appears that the sisters of twin-producing parents are more apt to have twins than the brothers of twin-producing parents; but the sisters of twin-producing fathers are more apt to have twins than the sisters of twin-producing mothers; also the brothers of twin-producing fathers are more apt to have twins than the brothers of twin-producing mothers. In all cases the proportion of twin births is very high, ranging from 4 to 7.5 times the average proportion of twin births in the whole population. These statistics then indicate that there is no important difference in the hereditary influence to twin production on the part of the father and the mother of offspring which include two or more sets of twins.

If, instead of considering the cases of twins in general, we pick out those of certain (or highly probable) *identical* twins, then we find, in 30 families with such twins, that the mothers came from fraternities in which (in 77 labors) there were 13 per cent. twin labors, and the fathers came from fraternities in which (in 38 labors) there were 13

per cent. twin labors. Here we see that there is an eqality of the maternal and paternal influence and that there is a larger proportion of relatives of *identical-twin* producers who are twins than of producers of *twins in general.* Indeed, the occurrence of twin-offspring to the fraternities of the parents of identical-twin producers is proportionally 12 times as common as in the population at large.

Another way of testing the inheritableness of 1-egg twins is by getting the frequency-distribution of the sex of twins in repeater families—those in which the influence of heredity most clearly shows itself. In these, therefore, we expect nearly an equality of twins of similar sex and of dissimilar sex, provided 1-egg twins are not found in these clearly inheritable strains. In 160 pairs of twins in repeater families, of which the sex is given, there are 54 of unlike sex and 106 of like sex. Expectation in the case of binovular twins is that there will be an equality of like and unlike sexed twins. Any excess of like-sexed twins is to be ascribed to the occurrence of 1-egg twins. In the present case, there is an excess of 52 pairs of like-sexed twins out of 160 pairs of twins, which indicates that about 1 in 3 of the twins in repeater families are identical twins, and this agrees approximately with statistics obtained from the population as a whole. From this we reach the conclusion that the tendency to production of 1-egg twins is certainly not less common in the case of repeater families than in the case of families in which there is only a single pair of twins. The statement, therefore, that there is no hereditary influence to be detected in the case of 1-egg twins appears certainly to be incorrect. In fact, the presence of heredity is more striking than in the case of other twins and this leads us to conclude that the hereditary tendencies toward uniovular multiple production so obvious in armadillo (*Tatusia*) persists also in man.

Still another way of testing the relative influence of the mother and father in twin production is the comparison of cases in which the father of twins has married twice, and the mother of twins has married twice. An examination of our records showed 30 families where at least one

parent of twins has married twice. In 14 cases it was the father who married twice, in 15 cases the mother, and, in 1 case, both father and mother. In the 14 cases of father of twins who had married twice, there were twins by both marriages in 2 cases, or 14 per cent. of all such cases. In the 15 cases where the mothers of twins had married twice, there were twins by both marriages in 3 cases, or 21 per cent. of all such marriages. The numbers are small, but, so far as they go, in view of the average occurrence of twins in only about 2 per cent. of all marriages (and hence if chance only were at work in 4 per 10,000 of both pairs of double marriages), they indicate that the tendency to twin production is hereditary and also that not only the mothers but also the fathers have great influence in determining the production of twins.

All the foregoing statistics speak strongly for the view that the father has about as much influence in the production of twins as the mother. This result at first sight seems quite inexplicable and indeed to reduce the whole matter to an absurdity. If twin production is due simply to double ovulation, what can the father have to do with the result?

The present paper does not attempt to give a final answer to this inquiry. It attempts only to set forth a hypothesis which suggests a line of experimentation to answer the question more definitely. We have assumed that 2-egg twins are due to the simultaneous bursting of two Graafian follicles while single births result from the bursting of a single follicle. There is, however, a good deal of evidence that single births are not always the consequence of the bursting of a single follicle merely. There are indeed several other factors that determine a single birth, such as the failure of one of two simultaneously expelled eggs to be fertilized or the failure of one of two simultaneously expelled fertilized eggs to develop to maturity. That is, it may well be that two eggs are simultaneously ovulated much more frequently than at present recognized and that the comparative rarity of twin-births is due either (1) to a failure of fertilization of one egg or (2) to a failure of development of one egg.

The conviction that not all eggs that are ovulated are fertilized is borne upon one who compares the number of corpora lutea in mammals that have large litters and the number of embryos that one finds in the uterus. I have recently made a number of counts in this respect in the case of sows and give below results in tabular form:

Observation Number	Number of Recent Corpora Lutea	Number of Embryos Found	Average Length of Embryos
1	3	3	15 cm.
2	6	3	10 cm.
7	8	7	6.5 cm.
12	9	2	2.5 cm.
13	8	7	
	34	22	

Thus from 34 corpora lutea, or 34 eggs expelled, only 22 embryos were found, counting only those which had reached a length of 2 cm., at which stage the chorion is already so large that it seems improbable that it should have been overlooked.

There is some reason for thinking that in humans also a certain proportion of the eggs ovulated fail of fertilization even in families in which there is no prudential restriction—in which the size of the families indicates a probability that nearly the maximum number of eggs became fertilized. Conclusions are fortified by the examination of a good genealogy including families of children born in the latter half of the eighteenth and the early part of the nineteenth centuries. Thus in a genealogy of the Gorton family, seventh generation, the intervals in round years between births in various fraternities (all related as cousins, are:

13 children—3, 1, 1, 5, 1, 2, 2, 2, 2, 2, 1, 5; all born 1795–1821.

10 children—2, 2, 2, 2, 2, 3, 2, 2, 2. In this case there is no unexpectedly large interval.

11 children—2, 2, 2, 2, 2, 2, 2, 2, 1, 5.

6 children—4, 2, 4, 3, 4; all born between 1792–1809.

8 children—2, 2, 2, 2, 2, 5, 2; all born between 1796–1813.

13 children—1, 2, 1, 2, 2, 2, 3, 3, 3, 2, 2, 4. In this case also

there seems to be no failure of fertilization, except at the end of the series.

9 children—4, 2, 2, 2, 2, 2, 2, 2.
10 children—3, 1, 4, 2, 1, 2, 2, 2, 2.
9 children—1, 2, 3, 4, 3, 2, 2, 3; born between 1825–1845.

One gets the impression that the normal interval between births, assuming all eggs to be fertilized, is about 2 years. The frequent intervals of 3, 4, 5 and even more years probably correspond to failure to fertilize, although they may be due to miscarriages or even in some cases to prolonged absence of the husband. In view of the fact, however, that we have to do here with a prevailingly rural population, chiefly farmers and millers in central New York State, the latter contingency is improbable.

The failure of fertilized eggs to complete their development is a real factor that must be taken into account. Attention has been called to the importance of this factor by John Hammond (*Journal of Agricultural Science,* VI, 1914) who has studied fetuses of rabbits and pigs and finds among them many degenerating individuals. Thus the number of degenerating fetuses in a large number of uterine horns examined varied from 0 to 19 per cent. I can confirm these results by observation made upon the uterus of a sow (No. 3) in which there were 2 corpora lutea in the left ovary and 5 in the right. In the left horn of the uterus there was a well-developed embryo 8 mm. long and one, evidently blighted, of 4 mm. The outlines of the latter embryo were highly abnormal and shrunken. The right horn of the uterus contained one embryo, 25 mm. long, a second 9 mm. long, and a third 6 mm. long. Thus with 7 corpora lutea in the ovaries, there were only 5 embryos found, of which one was completely blighted, another at 6 mm. length would probably soon have ceased development and two others at 8 and 9 mm. were far behind the best developed embryo, already 25 mm. long.

Work on yellow mice, of which the yellow $\times$ yellow matings give rise to 25 p. c. atretic embryos, and the far more extensive experience of Morgan with lethal factors in *Drosophila,* indicate that failure of development is a far

more common phenomenon than hitherto appreciated. Lethal factors, it may be pointed out, are a probable solution of one of the mysteries of gynecology; namely, that a woman who is sterile with one husband is often fertile with another, even when examination has shown no defect in the spermatozoa. Similarly a husband may have no children by one wife, but one or more by a second marriage. Parallel phenomena are common in dairy cattle. We conclude then that lethal factors are probably widespread phenomena even in human germ cells, and account for a certain proportion of long intervals between births, of early miscarriages, and of sterile unions.

The application of the foregoing two principles of failure of fertilization and failure of development to the question of the rôle of the male in twin production is now fairly obvious. More eggs are laid, even without prudential restraint, than come to development, and this is true not only of eggs laid successively but of eggs laid simultaneously; that is, twins that are born are the residuum of a greater number of twins that are started in their development and of a still greater number of pairs of eggs simultaneously ovulated.

The literature of gynecology is indeed full of cases of blighted twins. In a fairly large proportion of all twin births, one of the twins has remained at a stage of development of the third, fourth, or even earlier month. The fetus is often found compressed and flattened; the name is given of papyraceus twin. The number of blighted twins which have been referred to in the literature amounts to several score, but naturally is a very small proportion of the whole. The vast majority of blighted twins are simply lost unnoted with the afterbirth. A record is made only of the larger blighted fetuses; the others are entirely overlooked, since search is rarely made for undeveloped embryos in the afterbirth, and the birth is consequently regarded as a single one. We must believe that a certain proportion, perhaps a large proportion, of the fraternities which show two or three twin labors interspersed with single labors are those in which pairs of eggs

have been ovulated in each case, but one of the pair has failed to develop, either through failure of fertilization or early blighting.

Now the lethal factors show their influence first in certain combinations, just as in the matings of yellow × yellow mice. The $\frac{1}{4}$ of the embryos which die are those which are derived from germ cells containing the genes for yellow, whereas the other $\frac{3}{4}$ may develop fully. So we concude that among humans the cases of twin-repeating fraternities are those in which there are no or few lethal factors in the germ cells, so that there is a maximum fertilization and development of the eggs laid.[1] In the case of families comprising only one pair of twins, combined with a number of single births, it is probable that in other cases there had been a double ovulation but one of the pair had failed to develop. The additional fact to be taken into account is that twins are found in a higher ratio in large families than in small ones. Large families, however, connote high fertility of the male as well as the female. From all these facts we reach the conclusion that families which readily produce twins do so not only because in the mother the eggs were laid in pairs, but also because in the father the sperm is active, abundant and without lethal factors, so that the number of eggs fertilized and brought to full term approaches a maximum. To repeat, such fathers, experience indicates, belong to strains which are exceptionally fertile and in which twins are repeatedly produced both along male and female lines. Thus it comes about that the fathers of twins are about as apt to belong to twin-producing strains as mothers of twins and that twinning depends on constitutional—hereditary—factors on both sides of the house.

[1] F. H. A. Marshall (1910), "Physiology of Reproduction," p. 618, recognizes that certain abortions in sheep "may be due to a want of vitality on the part of the developing embryo." Similarly gynecologists recognize that a part of the 10 per cent. of barren marriages, and many of the early miscarriages, have no explanation in pathology, but apparently only in physiology.